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=> HIV

L1 176430 HIV

=> humanized (w) monoclonal (w) antibody

L2 1066 HUMANIZED (W) MONOCLONAL (W) ANTIBODY

=> L1 and L2

L3 20 L1 AND L2

=> gp120 and L3

L4 5 GP120 AND L3

=> D L4 IBIB ABS 1-5

L4 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:49959 CAPLUS

DOCUMENT NUMBER: 135:151297

TITLE: Virolysis and in vitro neutralization of HIV  
-1 by **humanized monoclonal**  
**antibody hNM-01**

AUTHOR(S): Nakamura, Mariko; Terada, Masaki; Sasaki, Hiroyuki;  
Kamada, Minoru; Ohno, Tsuneya

CORPORATE SOURCE: Department of Microbiology, Jikei University School of  
Medicine, Tokyo, 105-8461, Japan

SOURCE: Hybridoma (2000), 19(6), 427-434  
CODEN: HYBRDY; ISSN: 0272-457X

PUBLISHER: Mary Ann Liebert, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Antibody humanization by transplanting the complementarity determining region (CDR) to a human framework aims to reduce the response of the human immune system against a foreign mol. during passive immunization. We transferred the CDR from the murine monoclonal antibody (MAb) NM-01 to a human IgG frame. The humanized NM-01 (hNM-01) recognizes the same epitope on Human Immunodeficiency Virus type 1 (HIV-1) envelope as its murine progenitor, but with greater efficiency, and shows enhanced neutralization of HIV-1. We have shown that this increase in reactivity may be attributed to residue 4 of the humanized  $\kappa$  chain, where the presence of a methionine residue rather than the murine leucine appears to promote a more advantageous conformation of the antigen-binding site, perhaps via packing interactions with the  $V_{\kappa}$  CDR1. The capacity of humanized NM-01 to neutralize direct clin. isolates was also examined with the expectation that hNM-01 will prove suitable for development as a therapeutic agent. This reshaped antibody reacted with several clin. isolates of HIV-1 tested. Moreover, we proved the ability of this antibody of its activation of complement by flow cytometry and electron microscopy anal. Although hNM-01 alone was capable of neutralizing HIV-1, the presence of complement enhanced neutralization. The enhancement of complement activation was also observed in hNM-01 than murine progenitor. This finding supports a potential role for antibody-dependent complement-mediated virolysis and more effective neutralization in HIV-1 therapy.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:908511 CAPLUS

DOCUMENT NUMBER: 135:44922

TITLE: Targeting HIV-1 gp120 to the high affinity FC receptor (FCyRI, CD64) on myeloid antigen presenting cells: implications for enhancing vaccine responses

AUTHOR(S): Howell, Alexandra L.; Thacker, Tara N.; Li, Fang; Fiering, Steve; Graziano, Robert F.; Goldstein, Joel; Fanger, Michael W.

CORPORATE SOURCE: V.A. Medical Center, VT, 05009, USA

SOURCE: Current Topics in Virology (1999), 1, 61-70

CODEN: CTVUAG

PUBLISHER: Research Trends

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We prepared a fusion protein containing a **humanized monoclonal antibody** (mAb), mAb H22, with specificity for the human high affinity Fc receptor for IgG (FcγRI, CD64), fused to **HIV-1 gp120**. This fusion protein construct was produced by joining the cDNA for the full length H22 heavy chain gene in frame to the cDNA for **gp120**. This construct, which also expressed a selectable marker, was stably transfected into a murine myeloma cell line that expressed the previously transfected H22 kappa light chain. The resulting fusion protein, (H22 + **gp120**), was secreted from the myeloma cell line and was purified by affinity chromatog. Flow cytometric anal. revealed that H22 + **gp120** bound with high affinity via the Fab portion of H22 to CD64 expressed on monocytes and macrophages from both humans and human CD64-expressing transgenic mice. Western blot anal. revealed that the 390 kDa fusion protein reacted with both anti-human IgG and anti-**gp120** mAbs. Incubation of a monocyte cell line with this fusion protein at 37°C resulted in internalization of the complex as determined by flow cytometric anal. Immunization of human CD64 transgenic mice with the purified H22 + **gp120** fusion protein induced higher titers of anti-**gp120** serum antibodies compared to immunization of non-transgenic littermates. Targeting **gp120** to CD64-expressing antigen presenting cells (APC) in vivo may augment immune responses and enhance protective immunity.

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L4 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:25990 CAPLUS

DOCUMENT NUMBER: 130:80353

TITLE: Monoclonal antibodies which neutralize HIV-1 infection

INVENTOR(S): Chang, Tse Wen; Fung, Michael S. C.; Sun, Bill N. C.; Sun, Cecily R. Y.; Chang, Nancy T.

PATENT ASSIGNEE(S): Tanox, Inc., USA

SOURCE: U.S., 16 pp., Cont.-in-part of U.S. Ser. No. 767,533.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5854400	A	19981229	US 1992-950571	19920922
US 5981278	A	19991109	US 1991-767533	19910926
PRIORITY APPLN. INFO.:			US 1987-57445	B2 19870529

US 1987-137861 B1 19871224  
US 1991-767533 A2 19910926

AB Murine monoclonal antibodies and related products such as antibody fragments, immunotoxins, human and humanized antibodies are disclosed, all of which bind to the **gp120** protein on the envelope of **HIV-1**. These antibodies and related products neutralize **HIV-1**. They inhibit the infection of T cells, and also inhibit syncytium formation. Further, the antibodies are preferably group-specific and neutralize various strains and isolates of **HIV-1**. These antibodies have a variety of uses, including the treatment of AIDS and ARC, the prevention of **HIV-1** infection, as well as a diagnostic application, in that they can be used for assaying of unknown fluid samples for **HIV-1**.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1994:433148 CAPLUS

DOCUMENT NUMBER: 121:33148

TITLE: Design and construction of **humanized monoclonal antibodies** by model building using peptides with sequences similar to complementarity determining regions  
INVENTOR(S): Harris, Linda J.; Bajorath, Jurgen; Hsiao, Ku Chuan  
PATENT ASSIGNEE(S): Bristol-Myers Squibb Co., USA  
SOURCE: Can. Pat. Appl., 58 pp.

CODEN: CPXXEB

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2096860	AA	19931127	CA 1993-2096860	19930525
EP <u>578515</u>	A2	19940112	EP 1993-401328	19930524
EP <u>578515</u>	A3	19950510		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: US 1992-888233 19920526

AB A method for designing **humanized monoclonal antibodies** by comparative model building is described. The complementarity-determining regions of the antibody are sequenced and compared to the sequences in a database of human proteins; these sequences are then modeled and tested to produce a model of the humanized antibody. Genes for the humanized Ig subunits are then constructed and expressed. The method is demonstrated by preparing a humanized antibody to CD18. Sequences from a Vg germline protein were found to be very similar to the mouse monoclonal antibody 60.3 light chain variable region and sequences from a human monoclonal antibody to **gp120** of **HIV-1** were similar to the heavy chain variable region. The sequences were modeled to give minimal rms values for backbone deviation and the energy function. The genes for the two subunits were prepared by standard methods and expressed in Ag8.653 cells. The humanized antibody inhibited CR3 (CD11b/CD18)-mediated uptake of zymosan by neutrophils as effectively as the original murine antibody.

L4 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1992:529323 CAPLUS

DOCUMENT NUMBER: 117:129323

TITLE: The brightening prospect for AIDS vaccines

AUTHOR(S): Girard, Marc

CORPORATE SOURCE: Inst. Pasteur, Paris, 75724, Fr.

SOURCE: Uirusu (1991), 41(2), 129

CODEN: UIRUAF; ISSN: 0042-6857

DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English

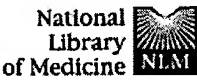
AB A review with no refs. in the field of AIDS vaccines. First, protection of chimpanzees against exptl. infection with HIV-1 was achieved by immunization of the animals with either the virus envelope glycoprotein gp120 alone or with a variety of antigens, among which the envelope glycoprotein gp160 and a synthetic peptide with the sequence of the HIV-1 principal neutralization determinant. The latter, the V3 loop of gp120, is a highly variable, type-specific determinant. Antibodies to the V3 loop neutralize virus infectivity at a late stage of virus penetration by blocking fusion between the viral envelope and the membrane of the target cell. Protection of chimpanzees against HIV infection was also using only gp160 as a vaccine. Vaccine protection can also be demonstrated against HIV-infected cells (cell associated virus). The presence of V3-specific neutralizing antibodies seems to correlate in all cases with protection against virus challenge, whether the virus is cell-free or cell-associated. Finally, a humanized monoclonal antibody to the V3 loop was able to provide passive protection to chimpanzees, thus confirming that the basis for protection against HIV infection lies in neutralizing antibodies.

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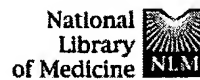
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<a href="#">#70</a>	Search CD4 binding site and V3 Field: All Fields	16:42:18	<a href="#">166</a>
<a href="#">#69</a>	Search CD4 binding site and V3	16:42:10	<a href="#">166</a>
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<a href="#">#48</a>	Search 2F5 and HIV and human monoclonal antibody Field: All Fields, Limits: Publication Date to 1993/12/30	13:46:28	<a href="#">3</a>
<a href="#">#46</a>	Search 2F5 and HIV and human monoclonal antibody Field: All Fields, Limits: Publication Date to 1994/12/20	13:45:45	<a href="#">6</a>
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<a href="#">#41</a>	Search 2F5 and HIV	13:44:28	<a href="#">90</a>
<a href="#">#40</a>	Search 2F5	13:44:22	<a href="#">173</a>
<a href="#">#38</a>	Search 2F5 antibody Limits: Publication Date to 1992/09/30	13:43:35	<a href="#">10</a>
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<u>#23</u>	Search humanized antibody and gp120	12:38:39	<u>14</u>
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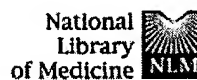
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for examination purposes, the claimed binding specificity of claims

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<a href="#"><u>#42</u></a>	Search <b>Paul DA and 1987</b> Limits: <b>Publication Date to 1994/01/06</b>	15:35:52	<a href="#"><u>12</u></a>
<a href="#"><u>#41</u></a>	Search <b>Paul DA</b> Limits: <b>Publication Date to 1994/01/06</b>	15:35:42	<a href="#"><u>30</u></a>
<a href="#"><u>#39</u></a>	Search <b>McDougal JS 1987</b> Limits: <b>Publication Date to 1994/01/06</b>	15:34:10	<a href="#"><u>4</u></a>
<a href="#"><u>#38</u></a>	Search <b>Tilley S 1991 and HIV</b> Limits: <b>Publication Date to 1994/01/06</b>	14:21:57	<a href="#"><u>1</u></a>
<a href="#"><u>#6</u></a>	Search <b>human monoclonal antibody and HIV gp120 and neutralize</b> Limits: <b>Publication Date to 1994/01/06</b>	10:59:19	<a href="#"><u>33</u></a>
<a href="#"><u>#9</u></a>	Search <b>GorMy C 1991</b> Limits: <b>Publication Date to 1994/01/06</b>	10:22:44	<a href="#"><u>33694</u></a>
<a href="#"><u>#8</u></a>	Search <b>Gorny C 1991</b> Limits: <b>Publication Date to 1994/01/06</b>	10:22:34	<a href="#"><u>0</u></a>
<a href="#"><u>#5</u></a>	Search <b>83D4 and 2G12</b> Limits: <b>Publication Date to 1994/01/06</b>	10:18:03	<a href="#"><u>1</u></a>
<a href="#"><u>#3</u></a>	Search <b>human monoclonal antibody and HIV gp120</b> Field: <b>All Fields</b> , Limits: <b>Publication Date to 1994/01/06</b>	10:17:22	<a href="#"><u>348</u></a>
<a href="#"><u>#1</u></a>	Search <b>panka and antibody</b>	09:32:18	<a href="#"><u>21</u></a>

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